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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,514	12/18/2001	Philip J. Barr	368292000200	6421

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EXAMINER	
WALICKA, MALGORZATA A	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,514	BARR ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *3,5-7,9,10,12-15 and 18-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8,11,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: copy of the papr by Otlewski et al..

The Amendment under 37CFR §1.111 filed on March 3, 2003, as paper No. 15, is acknowledged. The amendments to the specification and claims have been entered as requested. Claims 1-3 and 24 are amended. Claims 1-35 are pending; claims 1, 2, 4, 8, 11, 16, and 17 are the subject of this Office Action. Claims 3, 5-7, 9-10, 12-15, 18-35 are withdrawn from consideration as directed to the non-elected invention; see 37 CFR 1.142(b).

Detailed Office Action

1. Objections

Objections to clam 8 made in the previous Office Action, paper No. 12, are withdrawn because Applicants' arguments have been found persuasive.

2. Rejections

2.1. 35 U.S.C. 112, second paragraph

Claims 4, 8, 16 and 17 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reasons stated on the previous office Action, paper No. 12 and reiterated herein. The phrases "amino acid from about 1 to about 394 of alpha 1 antitrypsin " and "amino acid from about 1 to about 107 of secretory leukocyte protease inhibitor" render the claims indefinite.

The claims are directed to protease inhibitors fragments comprising amino acid residues acids 1- 394 of ATT and/or 1- 107 of SLPI, without giving the sequence identification number.

In addition, the term "about" in claims 4, 16 and 17 is a relative term, which renders the claims indefinite. The term "about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. It is unknown which amino acid residues are included and which are excluded from the scope of the invention, because applicants disclose the full sequences of human ATT and human SLPI from which SEQ ID NO: 2 and SEQ ID NO: 4 are taken.

In their traversal of the above rejection Applicants write, "It is not necessary to restrict the claim to a single sequence in order for a person of ordinary skill to interpret the metes and bounds of the claims. One of skill in the art, reading the claim in view of specification, would understand to mean human as well as other ATT and SLPI as well as any variants of these AATs and SLPs. See, e.g., specification paragraphs 59, 67, and 68."

Applicants' arguments have been fully considered but are found not persuasive. The polypeptide consisting of amino acids 1-394 or 1-107 remains indefinite as long as it is not identified by its sequence identification number, which is SEQ ID NO: 2 or SEQ ID NO: 4.

The phrases "amino acid from about 1 to about 394 of alpha 1 antitrypsin " and "amino acid from about 1 to about 107 of secretory leukocyte protease inhibitor" are indefinite as long as the particular variant of ATT and SLPI used to make invention are not disclosed. Human ATT is characterized by genetic polymorphism and the IDS

teaches that there are more than 50 allelic forms. In addition, recombinant human ATTs, as well as all variants of ATT from other animals are included in the scope of the claims. Similar comments apply to amino acids 1-107 of secretory leukocyte protease inhibitor. Amino acid 1-395 are not the same in all human allelic forms and in other all ATT, similarly amino acids 1-107 of SLPI are not the same in all human, animal and recombinant variants.

3.2. 35 U.S.C. 112, first paragraph

3.2.1. Lack of written description

Claims 1, 2, 8 and 11 are rejected under 35 U.S.C. 112, first paragraph, for the reason indicated in the previous office Action, paper No. 12 and reiterated herein.

The claims are directed to large and variable genera of fusion proteins.

Claim 1is directed to a genus of the fusion proteins encompassing proteins consisting of:

1) any protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof, and

2) any second protease inhibitor or a functionally active portion hereof,

wherein the fusion protein has protease inhibitor activity.

The scope of the claim encompasses a large and variable genus of fusion proteins, which comprise an alpha 1-antitrypsin inhibitor and protease inhibitor, or a functionally active fragments thereof, wherein both components of the fusion protein

originate form any natural and man-made source.

The description of the invention is insufficient, because the Applicants' intention is to produce a multifunctional, actually bifunctional, inhibitor, see the title of the disclosure, that has activities of both inhibitors, i.e. the activity of ATT and any other inhibitor that was used for construction of the fusion protein.

In their response Applicants write, on page 9, line 5, "one skilled in the art is apprised of Applicants' possession of the invention as claimed by the numerous sequences of protease inhibitors, and functionally active portions of protease inhibitors, that may serve as components of the fusion proteins of the invention."

This argument is found not persuasive, because Applicants' inventions are not protease inhibitors *per se*, but the fusion proteins thereof that are multifunctional. Therefore, the argument is relevant to the issue of enablement and not written description of the invention.

Applicants teach several representatives of the genus wherein the species have the function of both protease inhibitors and structure described by amino acid sequences of SEQ ID NOs: 8, 16, 10, 18, 14, 20 and 22. This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus of fusion proteins, because combination of any two inhibitors, or their functional parts, does not necessary lead to a fusion protein having the desired function specificities of both components. One skilled in the art realizes that the change of one amino acid of a protein my lead to its inactivation. Therefore, it is doubtful that any combination of two inhibitors as claimed will result in bifunctional fusion protein.

The specification fails provide the identifying structural characteristics of said genus.

In conclusion, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 2 is directed to a genus of the fusion proteins encompassing proteins consisting of:

1) any protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof, and

2) any secretory leukocytes protease inhibitor or a functionally active portion hereof,

wherein the fusion protein has protease inhibitor activity.

The scope of the claim encompasses a large genus of fusion proteins that comprise an alpha 1-antitrypsin inhibitor and secretory leukocytes protease inhibitor, as well as functionally active fragments thereof, wherein both components of the fusion protein originate form any natural and man-made source and wherein the wherein the fusion protein has protease inhibitor activity.

The description of the invention is insufficient, because the Applicants' intention is to produce a multifunctional inhibitor, see the title of the disclosure that has activities of both inhibitors, i.e. the activity of ATT and secretory leukocytes protease inhibitor.

Applicants teach only two representatives of the genus wherein the species

have the function of both protease inhibitors and structure described by amino acid sequences of SEQ ID NOs: 8 and 16 (SLAPI and reverse SLAPI). This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Combination of any two inhibitors, or their functional parts, does not necessary lead to a fusion protein having the desired function specificities of both components. Human ATT has more than 50 natural allelic forms, and the scope of the claim comprises any ATT including recombinant forms. Also SLPI is a generic protein and the genus comprises any variant of human and animal SLPI variant. One skilled in the art realizes that the change of one amino acid of a protein may lead to its inactivation. Therefore not any combination of ATT and SLPI will result in a fusion inhibitor having both functions. Thus, providing extensive disclosure of the component inhibitors, as Applicants argue on page 9, line 5, is not a substitute for disclosure of a genus of bifunctional inhibitors claimed in claim 2. The specification fails to provide the identifying structural characteristics of said genus.

In conclusion, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 11 is directed to a genus of the fusion proteins encompassing proteins consisting of:

1) any protease inhibitor comprising alpha 1-antitrypsin or a functionally active portion thereof, and

2) any serine protease inhibitor or a functionally active portion hereof,

wherein the fusion protein retains the function of inhibiting protease.

The scope of the claim encompasses a large and variable genus of fusion proteins that comprise any alpha-antitrypsin inhibitor and any serine protease inhibitor, as well as functionally active fragments thereof, wherein both components of the fusion protein originate form any natural and man-made source and wherein the fusion protein retains the function of inhibiting protease.

The description of the invention is insufficient, because the Applicants' intention is to produce a multifunctional inhibitor, see the title of the disclosure, that has activities of both inhibitors, i.e. the activity of ATT and activity to inhibit the other serine protease.

The disclosure also fails to teach structure of fusion proteins themselves. Applicants teach only two representatives of the genus wherein the species have the function of protease inhibitors of serine proteases. The structure is described by amino acid sequences of SEQ ID NOs: 8 and 16 (SLAPI and reverse SLAPI). This is, however, insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Serine proteases are grouped in more than 20 families of enzymes of different properties; see Table 1 in the enclosed review by Otlewski et al., (Protein inhibitors of serine proteinases, Acta Biochimica Polonica, 1999, 46, 531-565). Taking into account the fact that serine protease inhibitors are a large and variable genus of protein, it is not certain that any combination of ATT and a second serine protease inhibitor will result in a fusion inhibitor capable of inhibiting trypsin and the second serine protease.

Thus, providing extensive disclosure of the component inhibitors, as Applicants

argue on page 9, line 5, is not a substitute for disclosure of an identifying structural characteristics of the genus of inhibitors claimed in claim 11.

In conclusion, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

3.2.2. Scope of enablement

Rejection of claims 1, 2 and 11 made in the previous Office Action paper No. 12 is withdrawn because Applicants' traversal is found persuasive.

4. Conclusion

No claim is in conditions for allowance, but the claims contain allowable subject matter. Applicants are the first to produce bifunctional fusion protease inhibitors that are set forth by SEQ ID NO: 8 and 16. No prior art anticipates or fairly suggests the invention.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner

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